BLOOD CHANGES UNDER ETHYLENE ANÆSTHESIA*

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A few months before the publication of the preliminary report on ethylene by Luckhardt and Carter,[1] our attention was called by Dr. Dean Lewis to the lowered rate of increase of blood sugar in dogs when using this then new anæsthetic.

Banting gave the first injection of insulin on January 10, 1922, but, its general employment did not take place for several years later. This was due both to the reluctance with which the medical profession accepted it, as well as to the difficulty of obtaining a standardized product. During this period, after the introduction of ethylene, and before the universal acceptance of insulin, we had nine cases of diabetes on whom ethylene was employed for surgical complications. In seven of these cases there was a temporary rise of about 50 per cent. in the blood sugar, while, with two, there was a 10 per cent. decrease. The blood sugar in all nine cases returned in twenty-four hours to what it had been before operation. We had no comparison of a blood sugar study of a similar series of cases operated on with ether as the anæsthetic. However, all nine of these cases reacted more satisfactorily as regards their diabetes than had been our experience when using ether in similar cases.

Of course, the general employment of insulin has made any anæsthetic now comparatively safe as far as blood sugar is concerned. However, if one anæsthetic produces fewer and less marked changes in the blood chemistry than another, then such an agent has a definite field in surgery, not only in the diabetic but also in any badly handicapped patient—not to mention the lessening of discomfort in the post-operative recovery of the average patient.

No study was made of the acid-base balance and none of the CO_2 combining power, for many reports have already been made on these changes with the various anæsthetics. Nor have we made any studies of the effects of anæsthetics on the blood-cells, for, there are so many factors, such as infection, secondary anæmia, etc., entering in this field, that it would be impossible to properly estimate such results. In passing, it is worthy of note that an increase of the leucocyte count can apparently be due to a diabetic acidosis independent of any infection.

This fact is proven by the number of such cases reported, and by two cases admitted to Jefferson Hospital, Roanoke, Virginia, on whom insulin, for one reason or another, had been omitted in a diabetic patient, with not only the resulting coma, but also with the development of a very high leucocyte count. With the giving of insulin, the coma cleared up, and the

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leucocyte count returned very promptly to normal. Of course, the clinical importance of this observation is too obvious to more than mention, especially if one recalls the abdominal pains sometimes associated with diabetic acidosis.

A few months ago we started making a comparative study of the blood of patients who were given ethylene-oxygen anæsthesia in comparison with the blood of patients on whom other anæsthetics were employed. The major part of this comparison has been with ether, though ether in combination with ethylene; chloroform; nitrous oxide-oxygen and regional (sacral) anæsthesia have been compared in a few cases.

The changes in (a) blood sugar, (b) bleeding time, (c) coagulation time and (d) native complement have been studied and ethylene-oxygen compared with the other anæsthetics above mentioned.

These changes in the blood were studied not only in patients but a comparison was also made in dogs.

In all the patients there were three specimens of blood obtained from each case. The first specimen being obtained several hours before the anæsthetic started and without any breakfast. All patients, however, had morphia, grain ⅛ with atropine grain 1/150 about fifteen minutes before anæsthetic started. The second specimen procured just before the anæsthetic was discontinued. The third specimen acquired twenty-four hours after cessation of the anæsthetic.

In the ethylene group there were 100 patients who were given nothing except ethylene-oxygen. The average length of time for this group was thirty-six minutes, while the average increased percentage of blood sugar was 29 per cent. for first post-operative specimen, or .8 per cent. per minute.

With fifty-three ether cases the average length of time was forty-eight minutes, while the average increased percentage of blood sugar for the first post-operative specimen was 73 per cent. or 1.51 per cent. per minute.

From this it is seen ether increased blood sugar 46 per cent. more than ethylene per minute for the first post-operative specimen. In twenty-four hours, the blood sugar in both series returned to practically the same as it was pre-operatively.

With dogs this increase of blood sugar was even more marked with those animals taking ether. Briefly the average increase percentage of the first post-anæsthetic specimen was 185 per cent. greater with ether than with ethylene.

In 1924, Leake and Hertzman [2] experimenting with dogs, "found the changes in the blood sugar and alkali reserve in dogs under ethylene-oxygen anæsthesia much less in rate and degree than with either chloroform or ether."

From this comparison between the results on dogs and on human beings, it is seen this is but another illustration of the well-known fact too much reliance cannot be placed on animal experimentation. However, ether increased the blood sugar more than ethylene in both patients and dogs.

There is a rather general impression found amongst surgeons that both the coagulation and bleeding time is slightly, but temporarily, increased by

ethylene. Luckhardt and Lewis [3] thought *perhaps* oozing was a little more marked with ethylene than with other anæsthetics. In our series in both human beings and dogs this has not been found to be true. In fact, the average increase in patients per cent. per minute of ether over ethylene, as regards coagulation time, is 125 per cent. With dogs this was less marked, for, the average increase per cent. per minute of ether over ethylene was 110.4 per cent.

With bleeding time the percentage of ethylene decrease per minute over ether is .0014 per cent. in patients; while with dogs it was 3.8 per cent.

Straus and Rubin [4] concluded in their recent article on this subject:

"1. In twenty-five patients we found a definite decrease in the coagulation time during and shortly following the administration of ethylene anæsthesia.

"2. This decrease was short-lived. In most instances within twenty-four hours there was a return of the coagulation time to that noted before the introduction of narcosis.

"3. The bleeding time was also decreased."

Allen and Murray [5] do not believe from their observations of 2750 cases of ethylene anæsthesia, that the bleeding time is increased, though, they did not report any definite estimates. J. S. Horsley, Jr.,[6] in twenty-five consecutive ethylene anæsthesia cases made estimates of the coagulation time, before operation, at the close of operation, and seventy-two hours following operation, and came to the conclusion that coagulation time was not prolonged.

It is perfectly possible the cutaneous oozing which some surgeons believe is occasionally present with ethylene, might be due to the momentary cyanosis produced by the anæsthetist attempting to obtain relaxation just as the operation starts.

Deductions made from a study of the so-called native complement indicates there is less disturbance to this indicator of resistance with ether than with ethylene. This holds true both in the human being as well as dogs.

A detailed laboratory report follows this summary, though, of course, even in such a report many tables are necessarily omitted.

The following is a report of experimental work done by the laboratory staff of the Jefferson Hospital in 167 cases, to determine the effect of ether, ethylene and in a few instances other anæsthetics, on blood sugar, coagulation time, bleeding time and native complement.

The technic of Folin and Wu for blood sugars was used. This consisted in using the protein-free blood filtrate, alkaline copper solution, boiling six minutes, cooling, the addition of phosphomolybdic acid and distilled water, after which estimations are made in the Kober Colorimeter.

For coagulation time Howell's method was employed (4 to 5 c.c. of blood are withdrawn from a vein of the forearm, expelled at once into a clean glass tube and slightly tilted.) Coagulation time is that period elapsing between the time of withdrawal and the time when the clot is sufficiently formed to allow the tube to be inverted.

For bleeding time, Duke's method was used. This consists in cleaning

the finger with alcohol and then with a dry, sterile sponge. The finger is then punctured with a lancet and the time taken after the first drop is wiped away until bleeding ceases. Each drop as formed is absorbed with a piece of filter paper.

Complement, one of the indicators of resistance, was also studied. Titrations were made on each serum under the same conditions and at the same time. We began with .01 c.c. of serum, increasing to .08 c.c., or in some cases to .1 c.c. 5 c.c. of physiological salt solution, followed by the same amount of a 1 per cent. cell suspension were then added. The latter had been previously sensitized with an anti-sheep hæmolytic amboceptor. Normally there should be sufficient complement in .01 to .02 c.c. of serum to produce a complete hæmolysis of the sheep cells.

Patients were grouped according to anæsthetic, operation and the time in which anæsthesia was employed.

There were 100 patients having ethylene, 53 having ether, 8 regional, 1 N_2O and ether, 2 chloroform, 1 N_2O and ethylene.

The following is a summary of our findings, details of which will be found grouped separately and of which a second report is being made:

CASES IN WHICH ETHER AND ETHYLENE ANÆSTHETICS WERE EMPLOYED AVERAGED AS FOLLOWS:

Blood sugar	Ether	Ethylene
Average time	48 minutes	36 minutes
Average pre-operative	129 mgms.	140 mgms. Diabetics included
Average first post-operative	217 mgms.	182 mgms.
Average second post-operative	130 mgms.	142 mgms.
Average increase, first post-operative	88 mgms.	38 mgms.
Average percentage increase, first post-operative.	73%	29%
Average increase, second post-operative	1 mgm.	2 mgms.
Average percentage increase, second post-operative	.8%	1.4%
Average increase per minute, first post-operative.	1.51%	.8%
Average percentage increase of ether over ethylene of		.71 or 46%

It may readily be seen that the second post-operative estimations were practically the same as the pre-operative findings, neither anæsthetic appearing to alter the blood sugar to any marked extent twenty-four hours after operation.

Coagulation time	Ether	Ethylene
Average time	48 minutes	36 minutes
First post-operative, total increase	4½ minutes	5 minutes
First post-operative, average increase	.08 minutes	.05 minutes
First post-operative, average increase per minute	.0016	.0013
First post-operative, average increase per minute in seconds	.09	.04

First post-operative increase, coagulation time, per minute of ether over ethylene is thus 125 per cent.

Coagulation time	Ether	Ethylene
Second post-operative, total increase	11½ minutes	20 minutes
Second post-operative, average increase	.21 minutes	.2 minutes
Second post-operative, average increase per minute	.0043	.0055
Second post-operative, average increase per minute in seconds	.25 seconds	.33 seconds

Therefore second post-operative increase of coagulation time in ethylene over ether is 32 per cent.

Bleeding time	Ether	Ethylene
Average time	48 minutes	36 minutes
Total increase, 1st, post-operative	5.5 minutes	7.75 minutes
Average increase, 1st, post-operative	.103 minutes	.1175 minutes
Average increase per minute, first post-operative	.0021	.0021
Average increase per minute, first post-operative	.126 seconds	.126 seconds
Average percentage, increase per minute, first post-operative	.463%	.405%

Therefore there is a first post-operative average percentage increase per minute of ether over ethylene of .0014 per cent.

It may thus be seen that there was no practical increase from the standpoint of bleeding time in the first post-operative findings.

Bleeding time	Ether %	Ethylene %
Increase second post-operative	70	6.75
Average percentage increase, second post-operative	1.32	6.75
Average percentage increase per minute	.027	.187

Therefore, it may be seen from the above that there was a percentage increase in bleeding time of .85 of 1 per cent. per minute of ethylene over ether.

Complement.—For the first post-operative there was an average increase per minute under ethylene of .834 per cent. Ether showed a percentage average increase per minute of .7 of 1 per cent. It may be seen, therefore, that there is practically no difference in complement, though the balance of .1 of 1 per cent. is slightly in favor of ether.

In the second post-operative complements the average increase per cent. for ethylene per minute was .423 per cent., while for ether it is .135.

False conclusions from the above might be drawn that ether was better from the standpoint of complement by 21 per cent., though the type of operation, necessary shock following same, etc., plays a great part in the above percentages.

A similar study to show the comparative values of ethylene and ether was made on each of ten adult dogs. The animals were first anæsthetized with ethylene, held in this state of anæsthesia for twenty minutes, after which they were allowed to revive. Blood sugars, coagulation times and bleeding times were taken under identically the same conditions as in the first portion of this report concerning the human patients. The same animals were then allowed to rest for a week, at the end of which time they were again anæsthetized for a like period of time with ether anæsthetic and the same observations were made.

Blood sugar	Ether	Ethylene
Average time	20 minutes	20 minutes
Average pre-anæsthetic	131 mgms.	110 mgms.
Average first post-anæsthetic	236 mgms.	141 mgms.
Average increase, first post-anæsthetic	105 mgms.	31 mgms.
Average increase percentage first post-anæsthetic	80%	28%

The average first post-anæsthetic increase of ether over ethylene was 21 mgms., average increase percentage first post-anæsthetic, either over ethylene, 185 per cent.

Blood sugar	Ether	Ethylene
Average second post-anæsthetic	143 mgms.	95 mgms.
Average increase second post-anæsthetic	12 mgms.	Decrease 15.5 mgms.
Average increase per minute, second post-anæsthetic	.655	Decrease .775 mgms.
Average percentage increase per minute, second post-anæsthetic	.91%	Decrease .7%

Therefore the average decrease of ethylene percentage over ether percentage is 1.61 per cent. The average decrease of ethylene over ether per minute is .8 per cent., and the average per cent. decrease of ethylene over ether is 23 per cent.

Coagulation time	Ether	Ethylene
Average pre-anæsthetic	1.15 minutes	.95 minutes
Average first post-anæsthetic	1.7 minutes	.90 minutes
Average second post-anæsthetic	1.37 minutes	.8 minutes
Average percentage increase, first post-anæsthetic	48%	Decrease 5%
Average increase per minute, first post-anæsthetic	2.4%	Decrease .25%
Average percentage increase, second post-anæsthetic	1.9%	Decrease 15%
Average percentage increase per minute	.95%	Decrease .75%

The ether average *percentage* increase per minute over ethylene average decrease percentage per minute is 2.65 per cent., and the average increase per cent. per minute ether over ethylene is 110.4 per cent.

In the second post-anæsthetic, the ether average increase per minute over ethylene is 1.7 per cent. The *percentage* increase, therefore, of ether over ethylene per minute is 178 per cent.

Bleeding time	Ether	Ethylene
Average pre-anæsthetic	1.27 minutes	1.2 minutes
Average first post-anæsthetic	.925 minutes	.6 minutes
Average second post-anæsthetic	.110 minutes	1 minute
Average percentage decrease, first post-anæsthetic	27%	48%
Average percentage decrease, per minute, first post-anæsthetic	1.3%	2.4%
Average percentage decrease, second post-anæsthetic	13%	16%
Average percentage decrease per minute, second post-anæsthetic	6.5%	.8%

The decrease per cent. ethylene was 21 per cent. The ethylene decrease per cent. per minute was 1.05 per cent. The percentage of ethylene decrease over ether decrease is 77 per cent. and the percentage of ethylene decrease per minute over ether decrease is 3.8 per cent.

Complement	Ether	Ethylene
Average time	20 minutes	20 minutes
Average pre-anæsthetic	.047	.042
Average first post-anæsthetic	.049	.047
Average second post-anæsthetic	.048	.048
Average percentage increase, first post-anæsthetic	.42%	1.19%
Average percentage increase, first post-anæsthetic, per minute	.021%	.059%
Average percentage increase, second post-anæsthetic	.28%	1.428%
Average percentage increase, second post-anæsthetic per minute	.014%	.0714%

Average per cent. increase of first post-anæsthetic, ethylene over ether, 183 per cent. Average increase second post-anæsthetic, ethylene percentage over ether percentage, .057 per cent. Average percentage increase, second post-anæsthetic, ethylene over ether, 407 per cent.

The following is a summary of the average increases and decreases of the various other anæsthetics which were used in our human cases, as compared to ethylene. The tests were run in identically the same manner and under the same conditions as those mentioned under ether and ethylene alone.

ETHYLENE AND ETHER

Blood sugar.

First post-operative-average increase per cent. per minute..... .5%
Second post-operative-average increase per cent. per minute..... .7%
First post-operative-average increase per cent. of ethylene over ethylene and ether 3%
Second post-operative-average decrease per cent. of ethylene over ethylene and ether ..... .68%

Coagulation time.

First post-operative-average decrease per minute ..... .05 or .06%
Second post-operative-average increase per minute ..... .001 or .03%
First post-operative-average increase ethylene over ethylene and ether ..... .0513 or 590%
Second post-operative-average increase ethylene over ethylene and ether ..... .004 or 400%

Bleeding time.

First post-operative-average increase per minute ..... .001 or .3%
Second post-operative-average decrease per minute ..... .001 or .3%
First post-operative-average per cent. increase per minute, ethylene over ethylene and ether ..... .15 or 37%
Second post-operative-average per cent. increased per minute, ethylene over ethylene and ether ..... .4 or 213%

Complement.

First post-operative-average increase per minute ..... .33%
Second post-operative-average increase per minute ..... .01%
First post-operative-average per cent. increase per minute of ethylene and ether over ethylene of ..... .271%
Second post-operative-average per cent. increase per minute of ethylene over ethylene and ether of ..... .0614%

REGIONAL

Blood sugar.

First post-operative-average increase per minute ..... 1.04 mg. or 173%
Second post-operative-average increase per minute ..... .16 or .11%
First post-operative-average increase per minute, ethylene over regional ..... .01 or .07%
Second post-operative-average increase per minute, regional over ethylene ..... .105 or .72%

Coagulation time.

First post-operative-total decrease ..... 3.5 minutes or 74%
First post-operative total increase ..... 2 minutes or 95%
First post-operative-total decrease ..... 1.5 minutes, or increase total 21%

First post-operative-average decrease per minute	.044 or inc. .026%
Second post-operative-average increase per minute	.0045 or 49%
First post-operative-average decrease per cent. per minute, regional over ethylene	.074%
Second post-operative-average decrease per cent. per minute, regional over ethylene	1.02%

Bleeding time.

First post-operative-average increase per minute	none
Second post-operative-average increase per minute	none
First post-operative-average decrease per minute, regional over ethylene	.405%
Second post-operative-average decrease per minute, regional over ethylene	.18%

Complement.

First post-operative-average increase per minute	.0023 or 1.672% (no decrease)
Second post-operative-average increase per minute	.00029 or 2.65%
First post-operative-average increase per minute, regional over ethylene	.838%
Second post-operative-average increase per minute, regional over ethylene	2.227%

SUMMARY

Finally we believe ethylene-oxygen anæsthesia produces: (a) Less alteration of the percentage of blood sugar, no appreciable change in either; (b) the coagulation time, or (c) the bleeding time, and (d) only a slight disturbance of the native complement when compared with any other of the now commonly employed anæsthetics. However, the whole study of blood changes under any anæsthetic is apparently dependent on the amount of oxygen in the circulation therefore, the anæsthetic chosen for the individual case should be the one that gives less cyanosis with a comfortable relaxation and does this in that particular hospital where it is to be employed.

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